

Figure 1

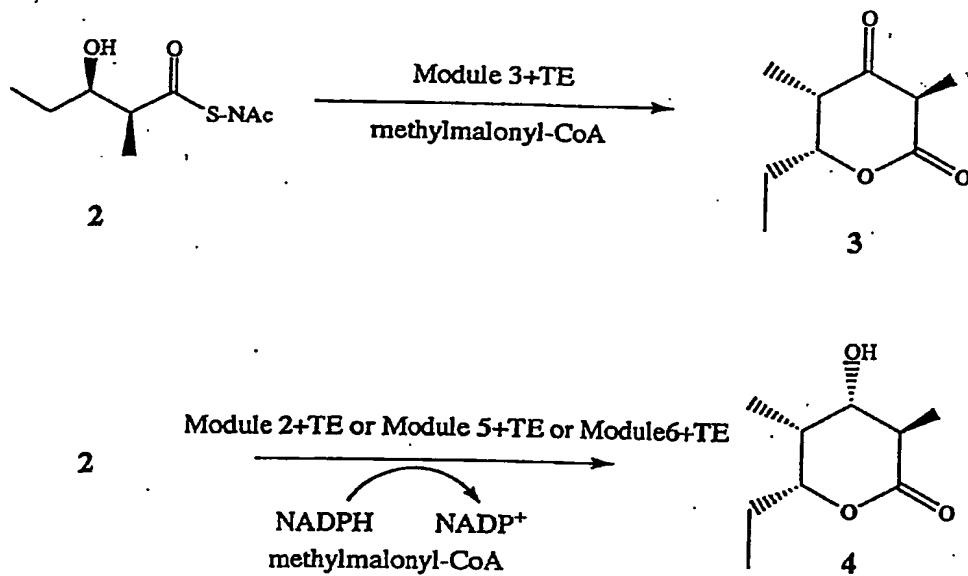


Figure 2

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(a) INTRA-POLYPEPTIDE LINKER

M2ery: GGATGAEQAAPATT..APVD
M4ery: VGDAD..QAA.VRVVGAA.DES
M6ery: VGAAEAEQA.PALVREVPKDAD
M2rif: FGSA.A.NR.PAEIGTAAAE
M3rif: LG..ER.PAAPAPVTRDVSD
M5rif: GETVAGAPATPVTTVADAG
M3rap: .ELFTGENPAPVRGPVSAVGQD
M4rap: .ELFTGENPAPVRGPVSVVGQD
M7rap: .ELFTGENPAPVRGPVSA.GQD

(b) N-TERMINAL INTER-POLYPETIDE LINKER

M3ery:VTD SE KVAEYLRR .ATLDLRAAR QRIRE..LES
M5ery: MSGDNGM.TE E.KLRRYLKR TVT.E LDSVT ARLRE..VEH RAG
M4rif:MSAPNE QIVDAL.R ASLKE....N VRLOQENSAL AAAAA
M7rif:VSASYE KVVEAL.R KSLEE....V GTLKKNRQL ADAAG
M8rif:V.AD EGQLRDYLKR .AIADARDAR TRLRE..VEE QAR
M9rif:MATD E.KLLKYLKR .VTAELHS... .LRKQGARH .AD
M5rap:MR.. EDQLLDAL.R KSVKE....N ARLRKANTSL RAAMD
M11rap:M.PEQD KVVEYL.R WATAELHTTR AKL.....EA LAAANT

Figure 3

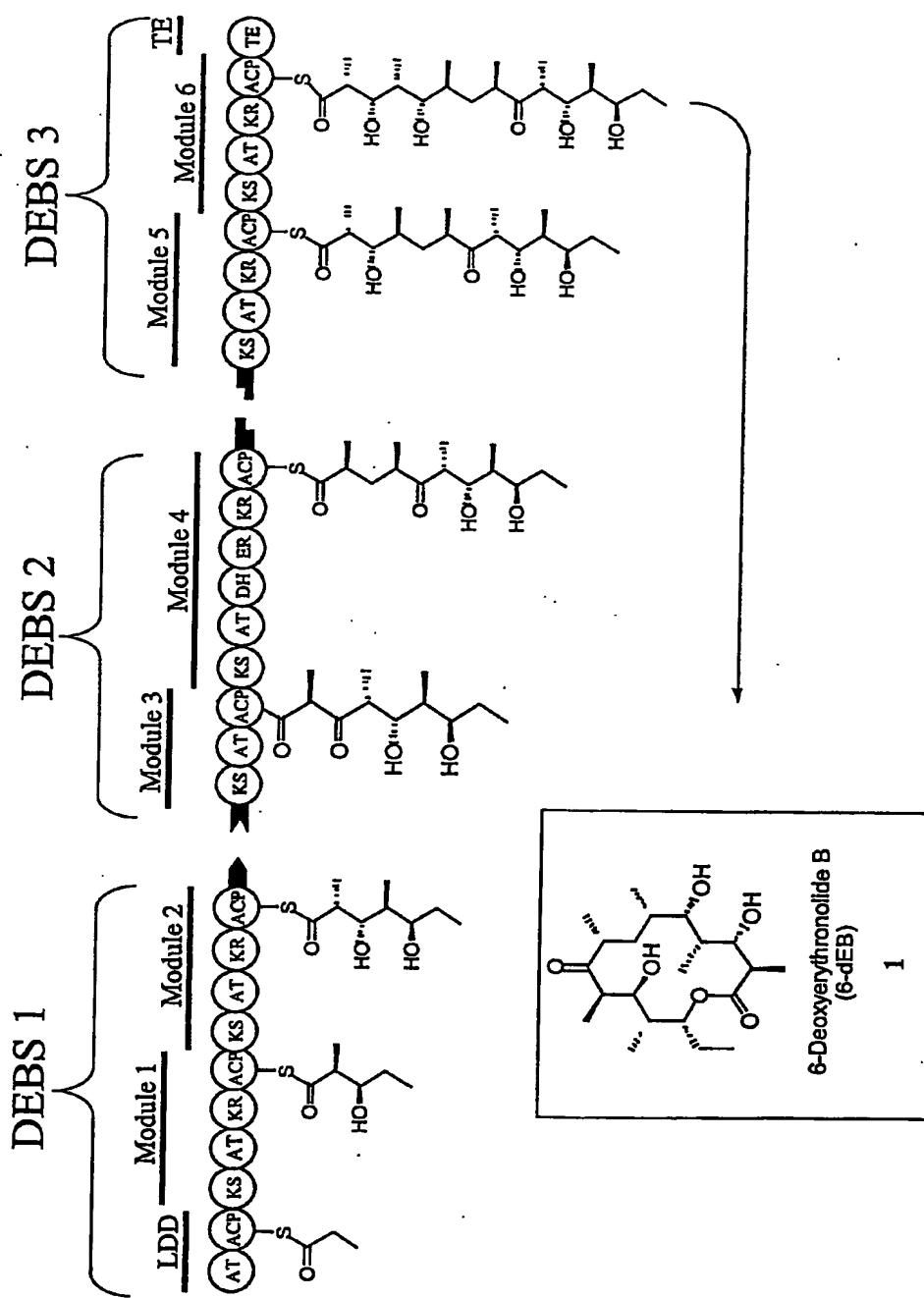


Figure 4

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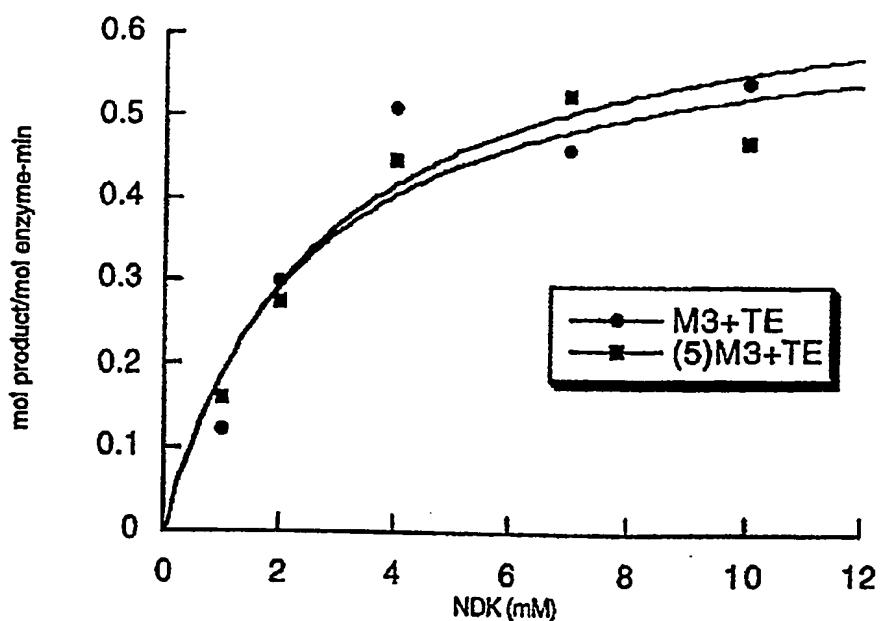
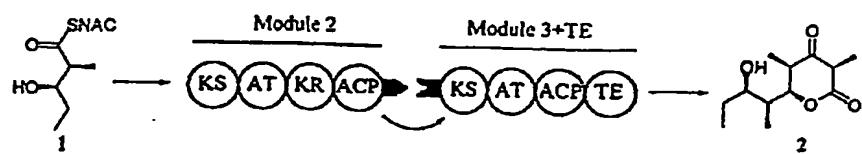
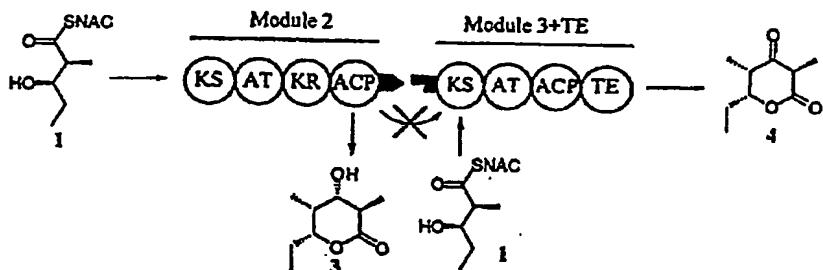


Figure 5

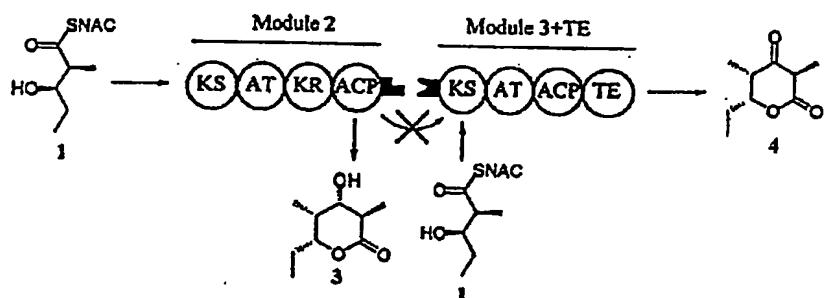
A. M2 and M3+TE



B. M2 and (5)M3+TE



C. M2(4) and M3+TE



D. M2(4) and (5)M3+TE

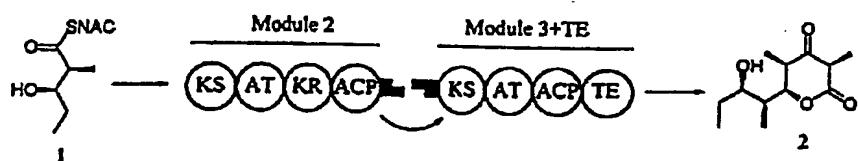


Figure 6

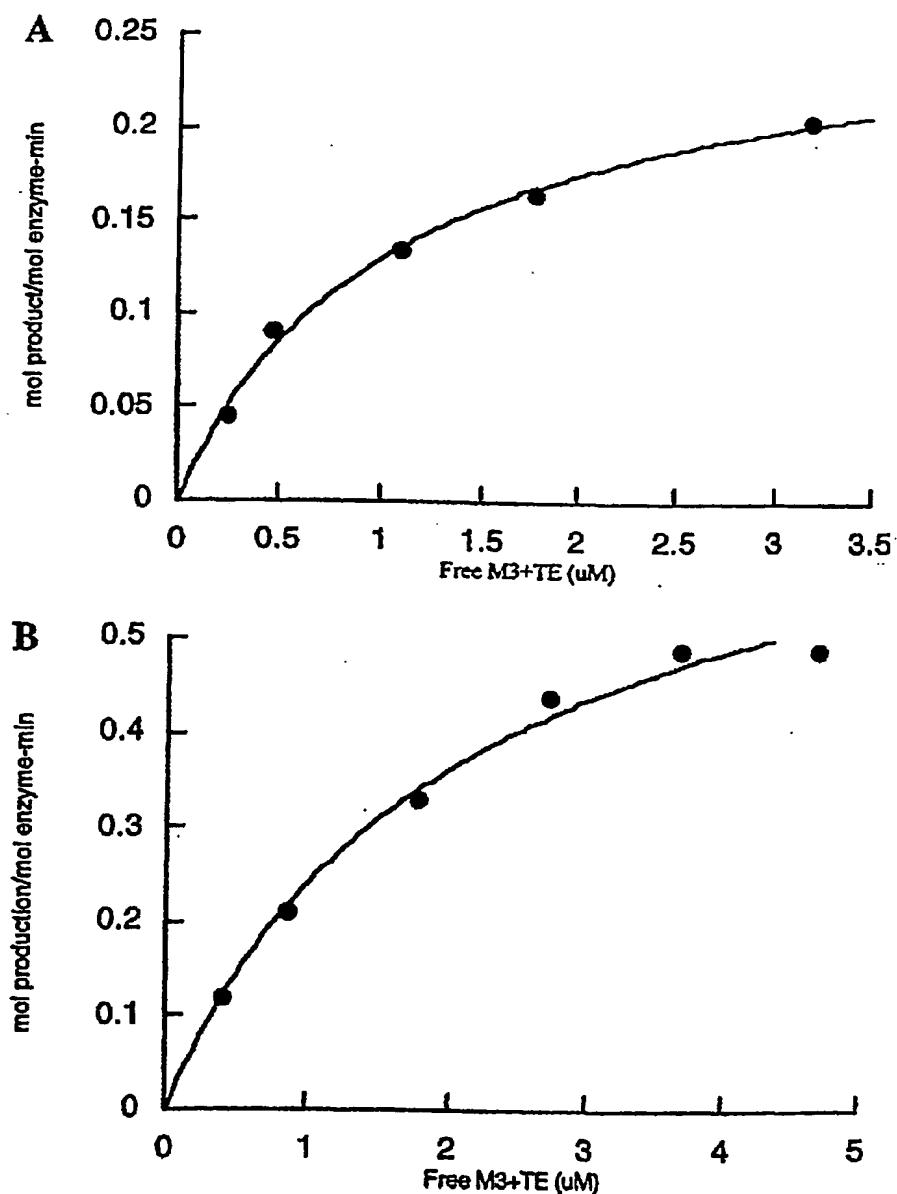


Figure 7

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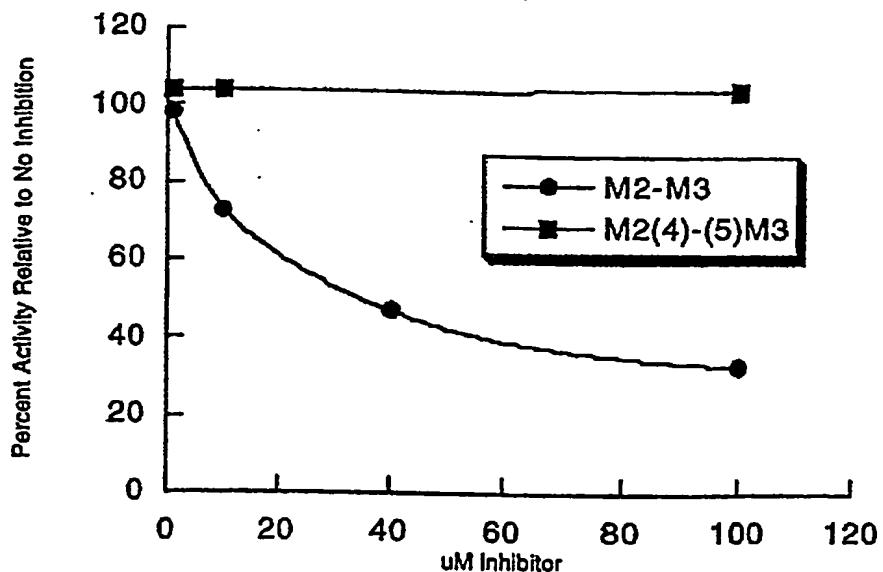


Figure 8

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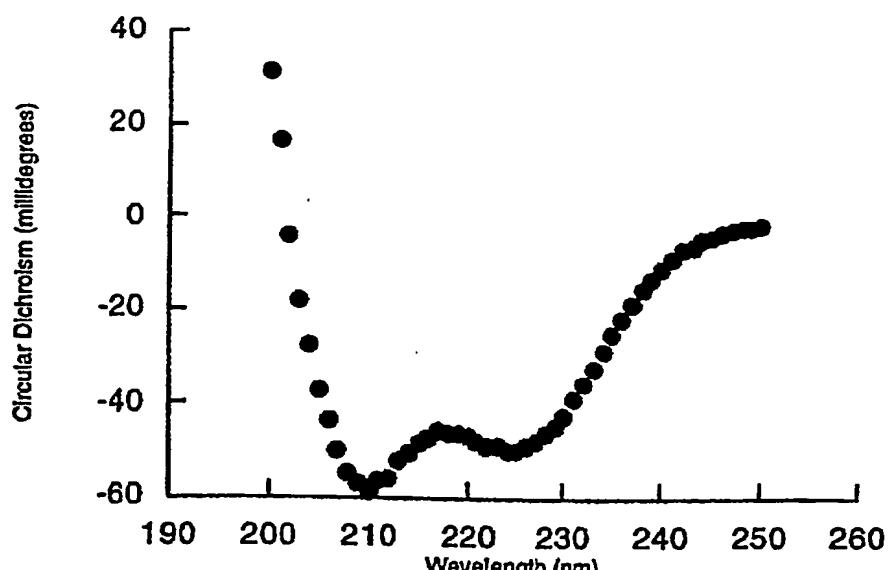
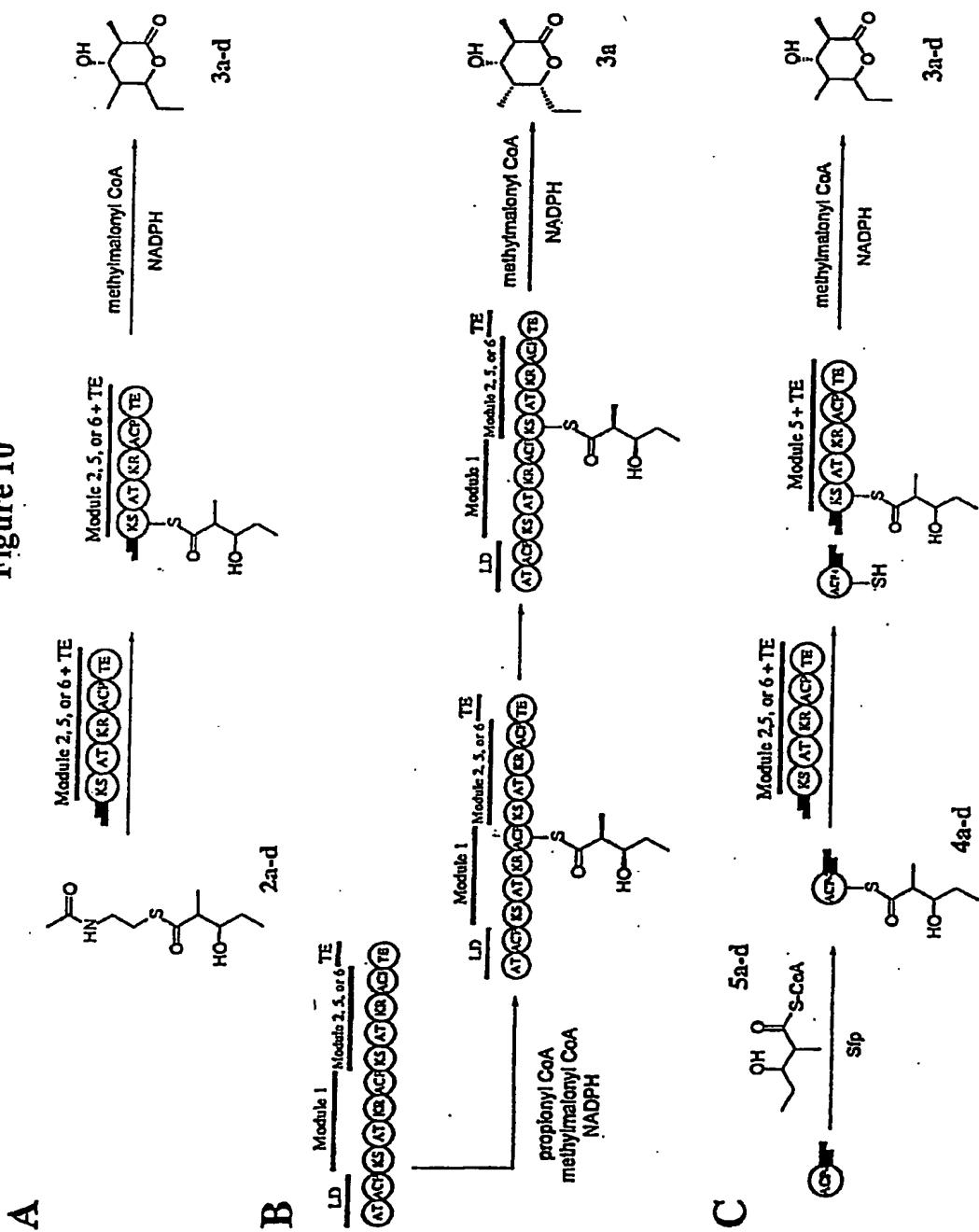
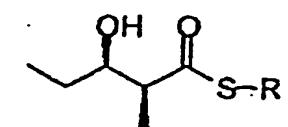


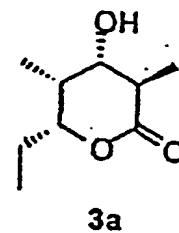
Figure 9

Figure 10

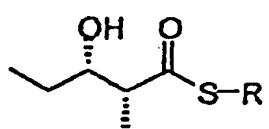




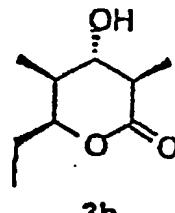
2a: R=N-acetylcysteamine
4a: R=AcyI carrier protein



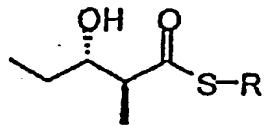
3a



2b: R=N-acetylcysteamine
4b: R=AcyI carrier protein



3b

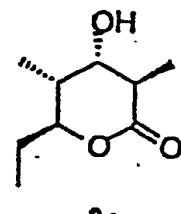


2c: R=N-acetylcysteamine
4c: R=AcyI carrier protein

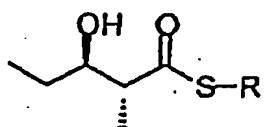
Module 2+TE
or
Module 5+TE
or
Module 6+TE

→ → →

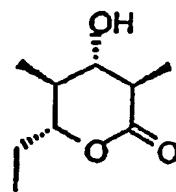
methylmalonyl CoA
NADPH



3c



2d: R=N-acetylcysteamine
4d: R=AcyI carrier protein



3d

Figure 11

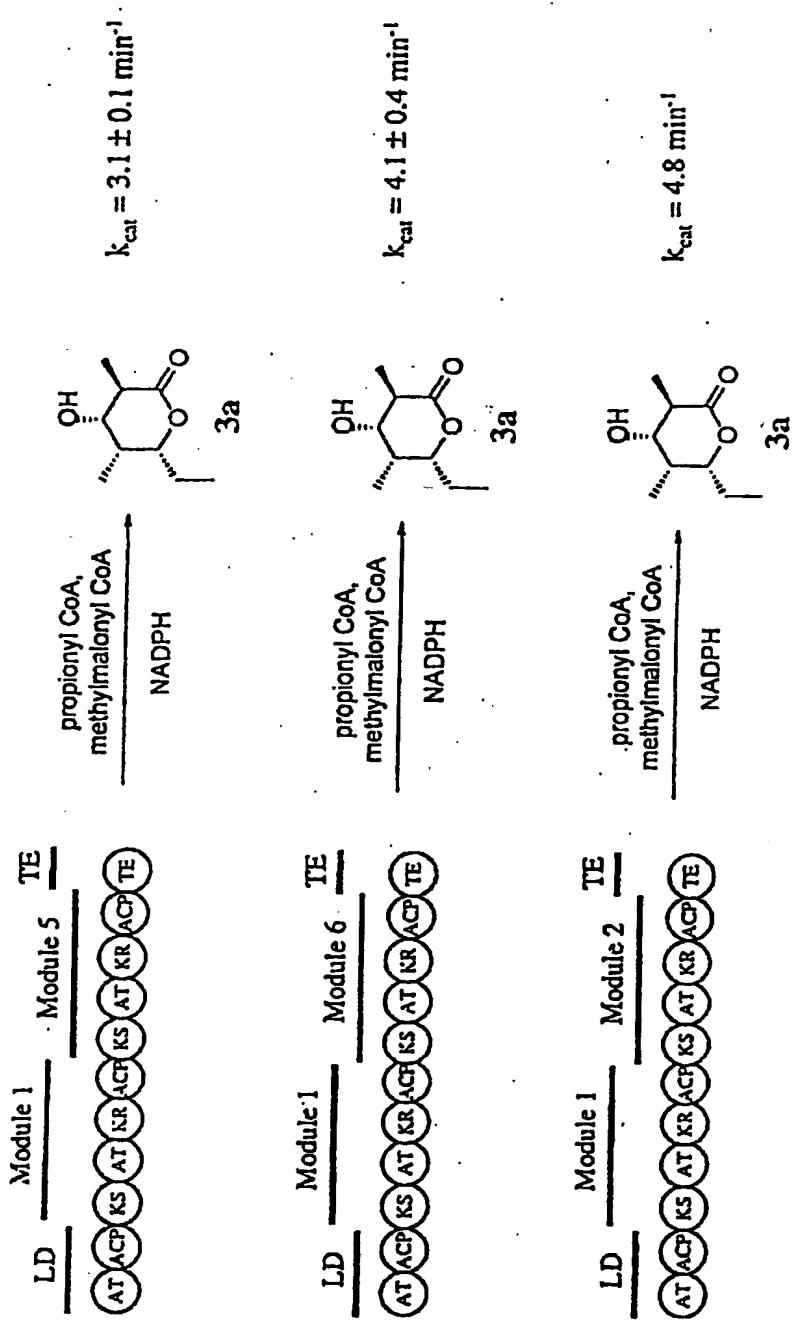


Figure 12

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Substrate	(5)Module 2 + TE KS AT KR ACP TE	(5)Module 5 + TE KS AT KR ACP TE	(5)Module 6 + TE KS AT KR ACP TE	
4a		2900 ± 500	290 ± 50	340 ± 60
4b		18 ± 1	3.9 ± 0.7	85 ± 15
2a		0.75 ± 0.01	0.016 ± 0.002	"1.1 ± 0.1
2b		0.0076 ± 0.0006	0.0011 ± 0.0001	0.058 ± 0.006

Figure 13

Substrate	(S)Module 2 + TE		(S)Module 5 + TE		(S)Module 6 + TE	
	KS AT KR ACP TE	KS AT KR ACP TE	KS AT KR ACP TE	KS AT KR ACP TE	KS AT KR ACP TE	KS AT KR ACP TE
4a		6.7 ± 0.2	> 9.3 ± 1.4	> 10 ± 1		
4b		> 0.97 ± 0.02	> 0.48 ± 0.02	> 3.4 ± 0.4		
4c		> 1.0 ± 0.1	> 1.4 ± 0.1	> 2.1 ± 0.2		
4d		> 0.29 ± 0.03	> 0.20 ± 0.01	> 1.9 ± 0.1		
2a		> 4.6 ± 0.6	0.24 ± 0.01	17 ± 2.9		
2b		0.25 ± 0.02	0.017 ± 0.001	2.4 ± 0.2		
2c		N. D.	N. D.	N. D.		
2d		N. D.	N. D.	N. D.		

Figure 14

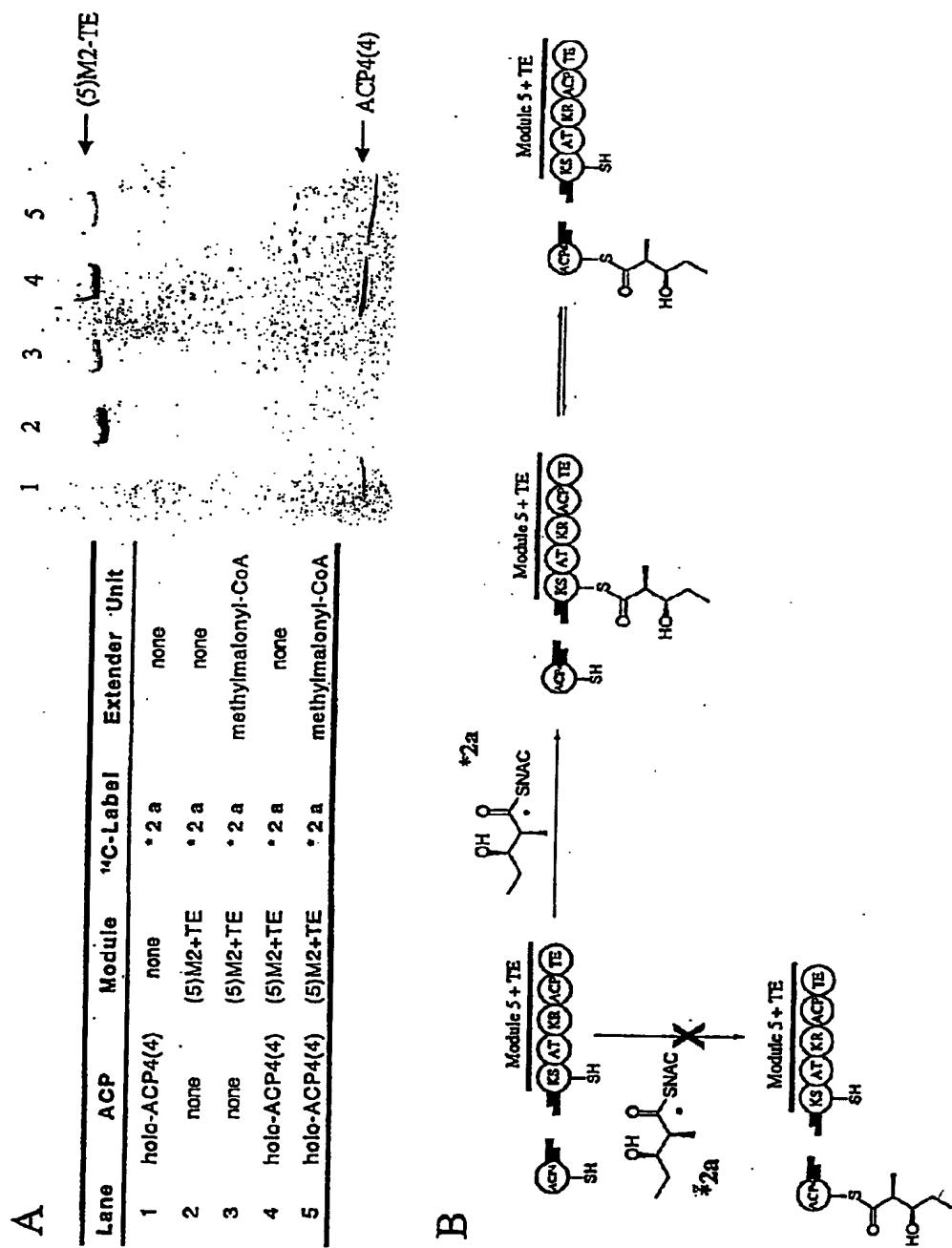


Figure 15

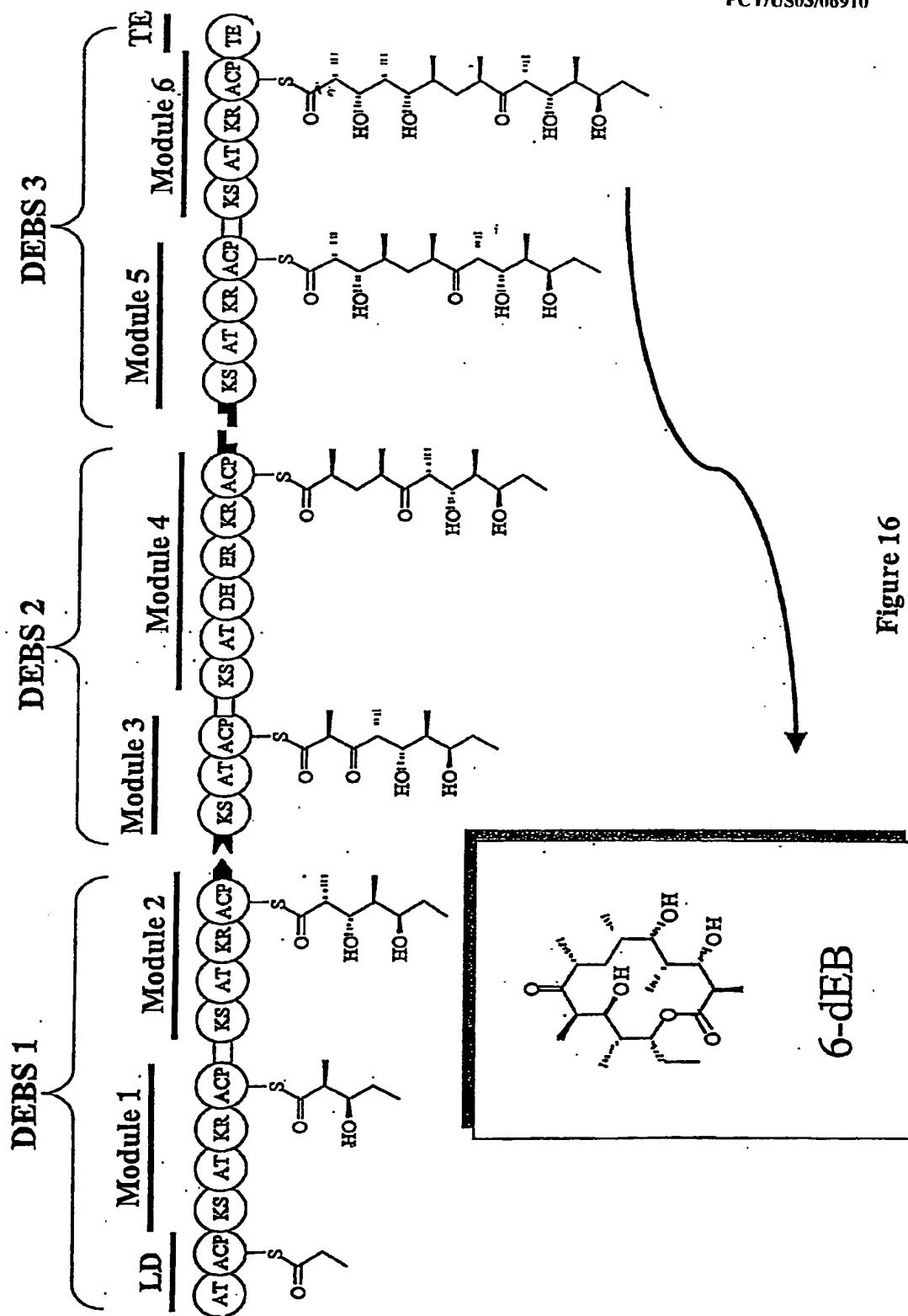
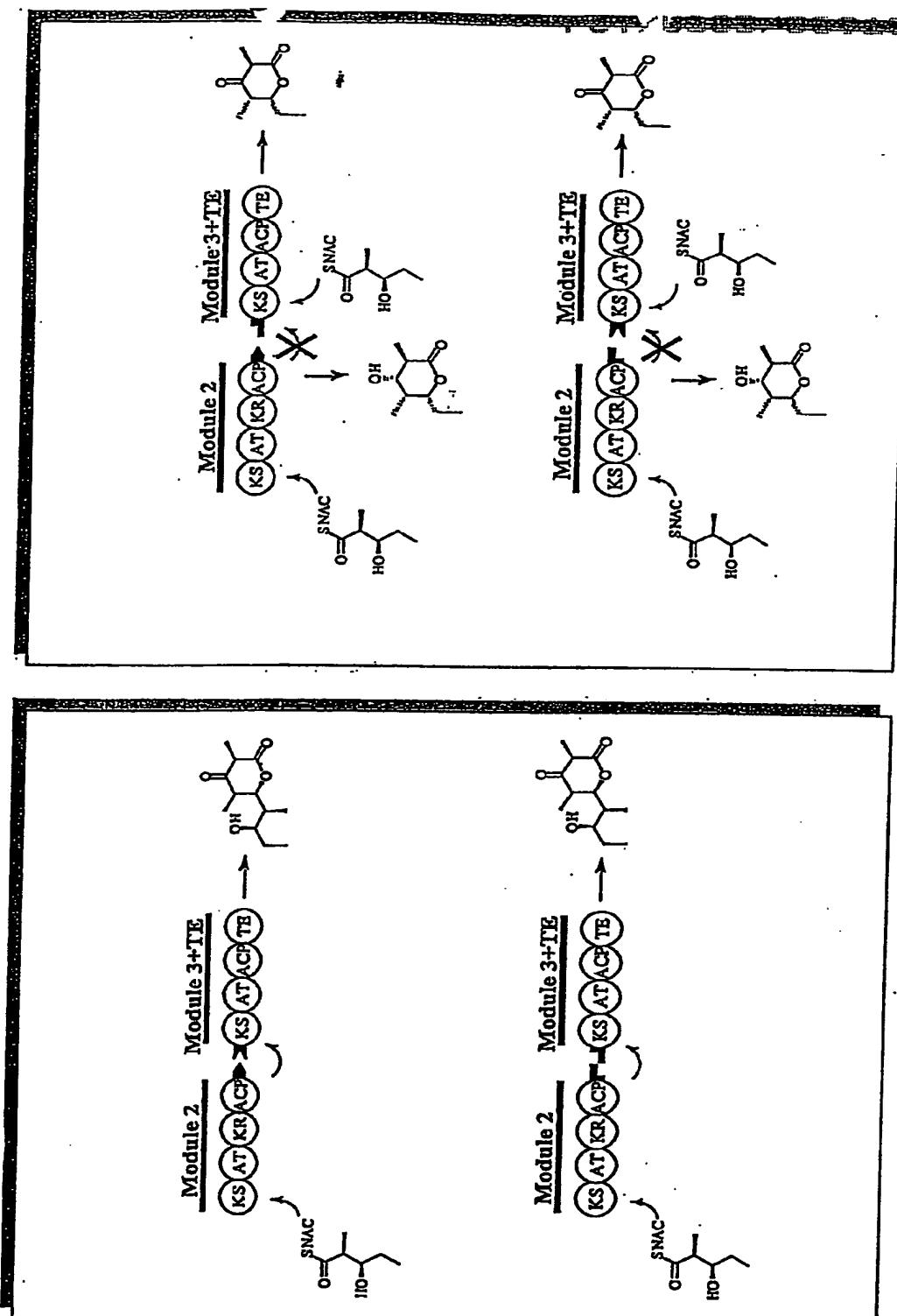


Figure 16



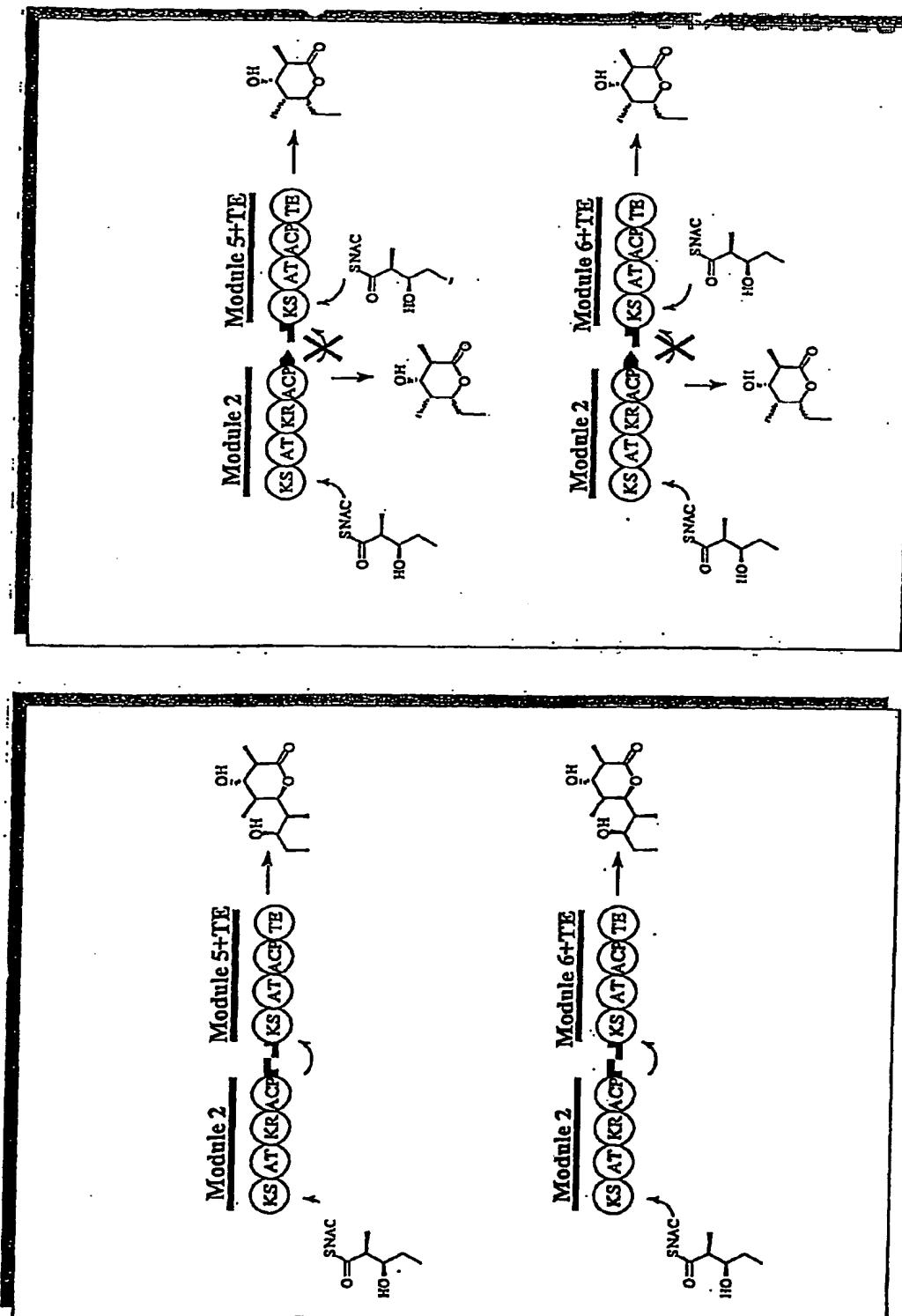


Figure 18

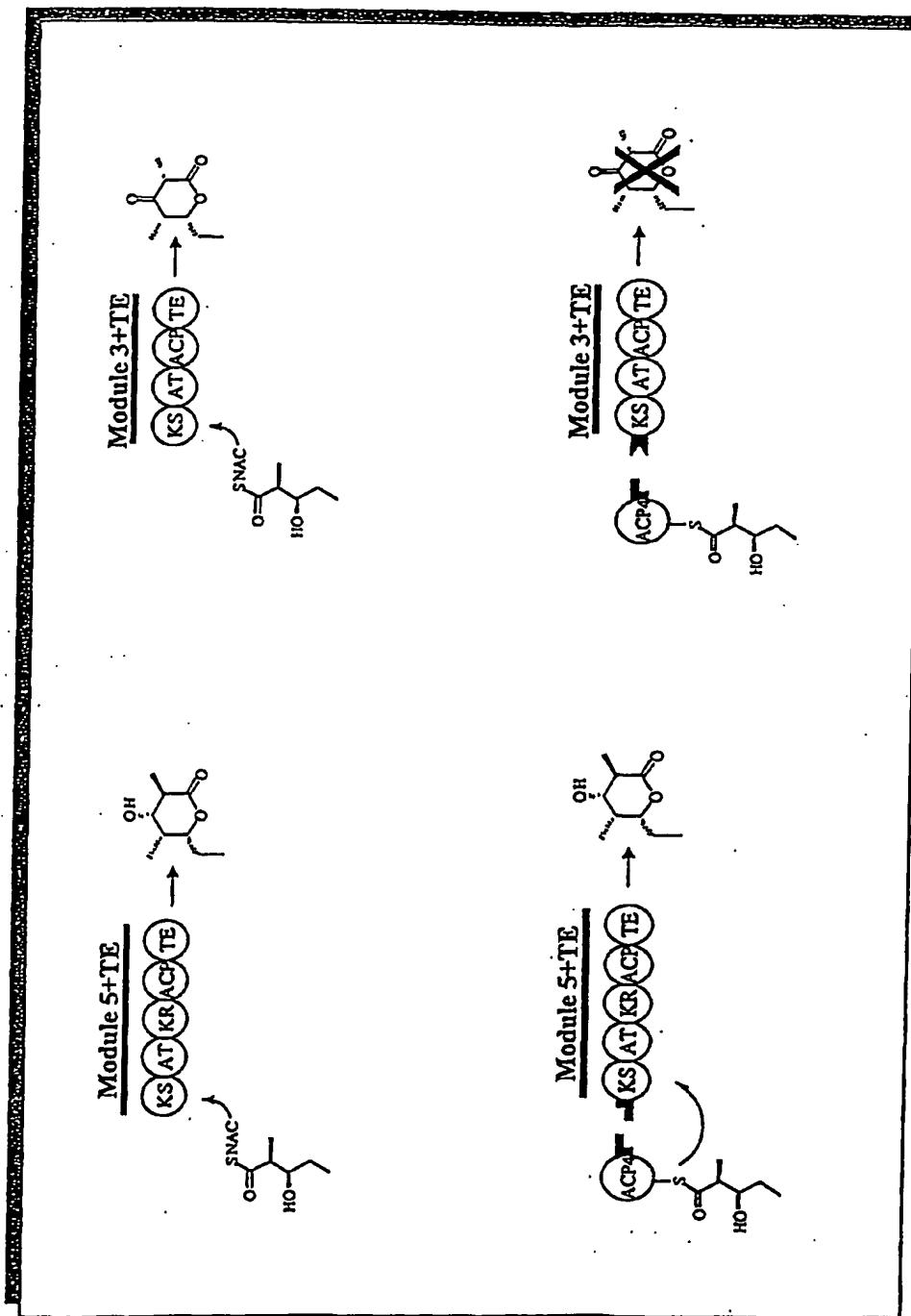


Figure 19

Figure 20

Enzyme \ Substrates						
Module 2 + TE 				X		
Module 5 + TE 					X	

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Figure 21

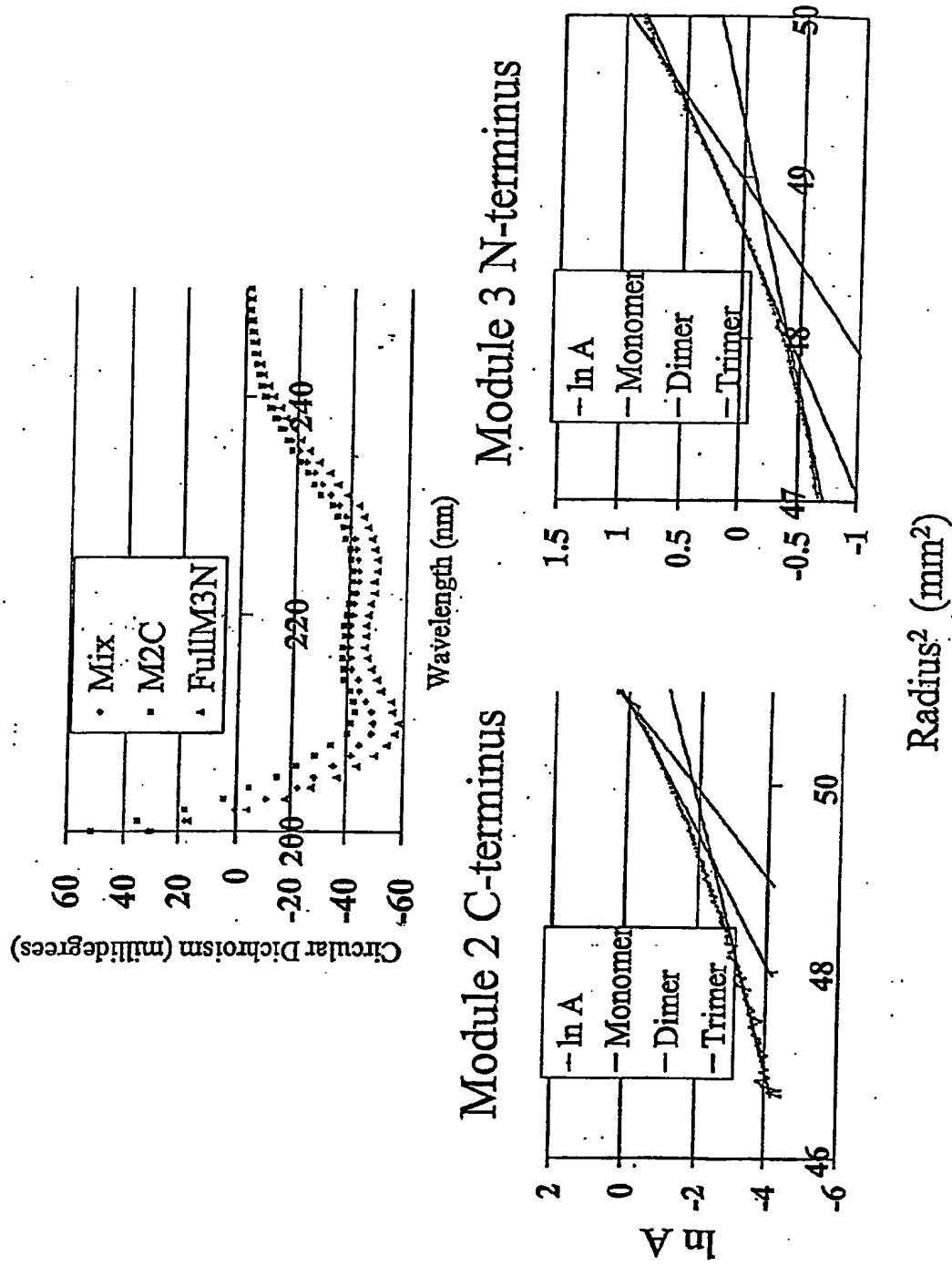
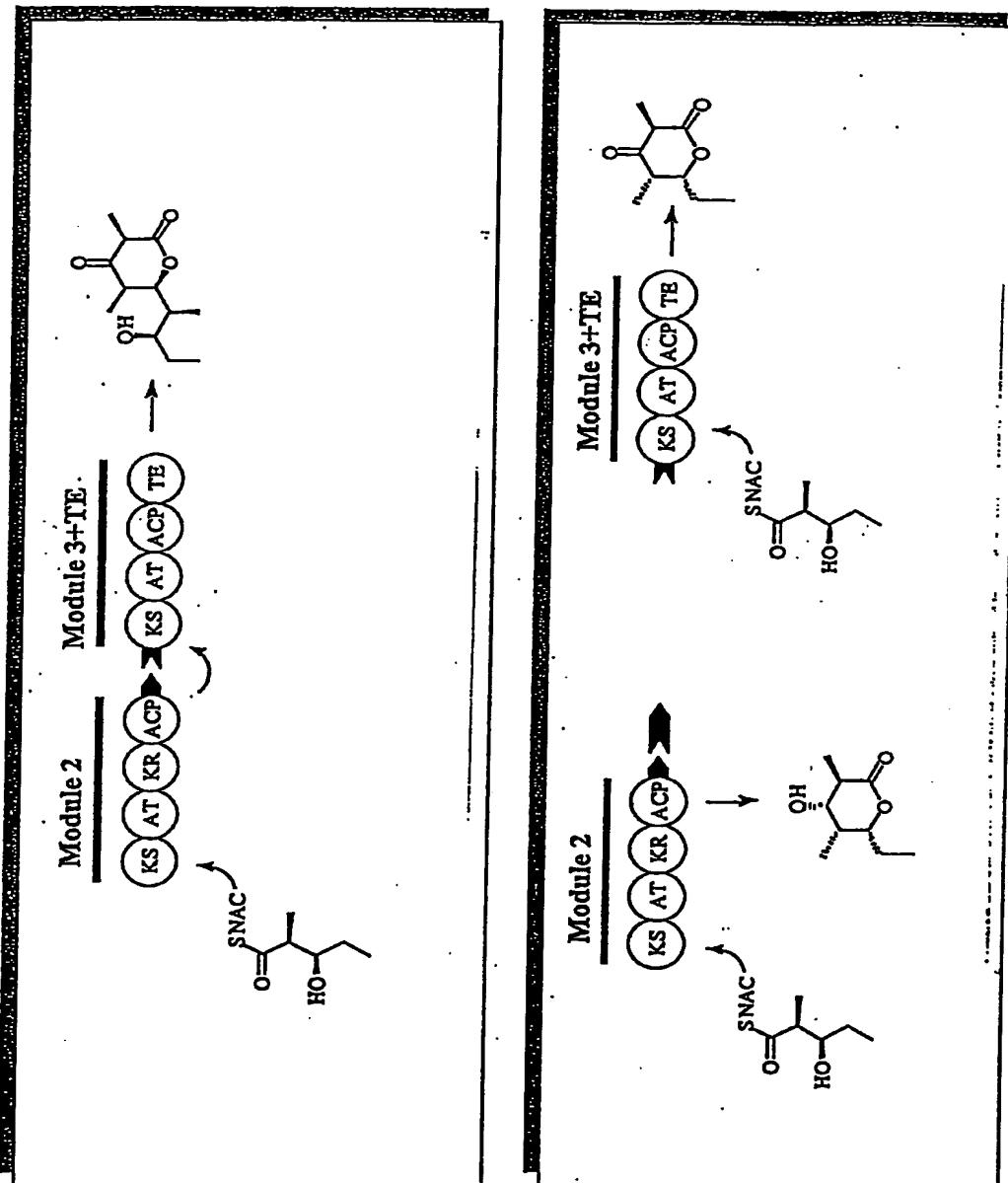


Figure 22



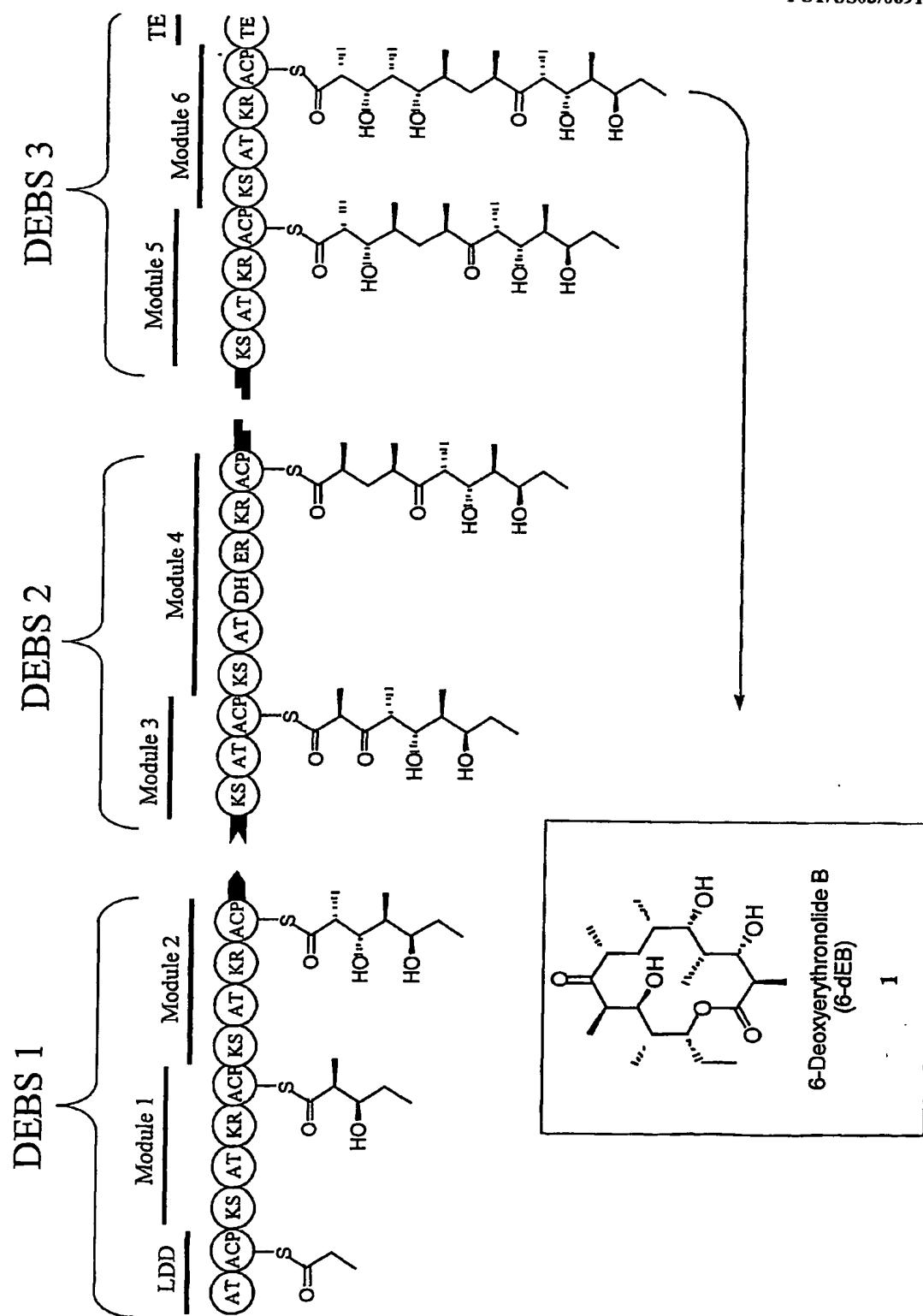


Figure 23

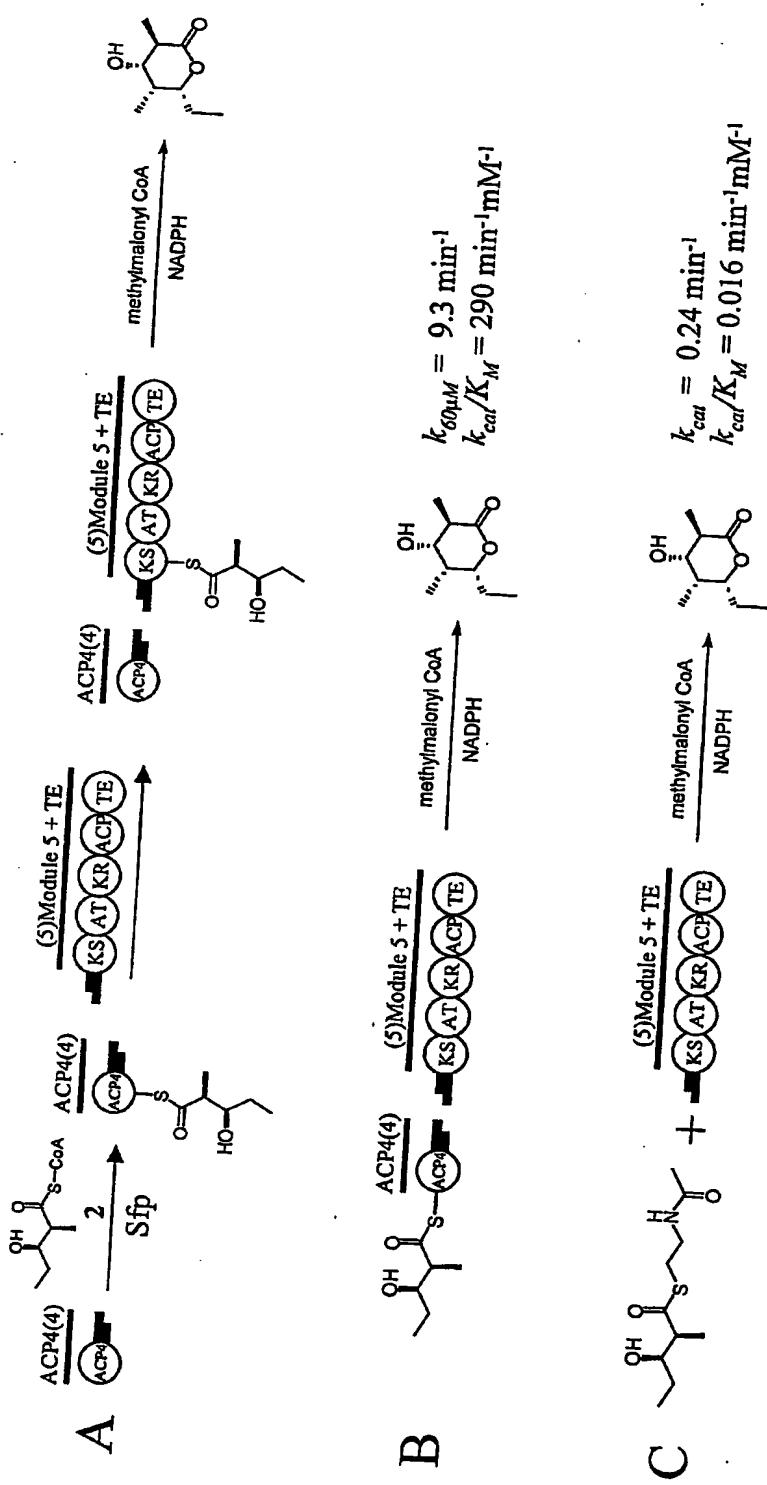


Figure 24

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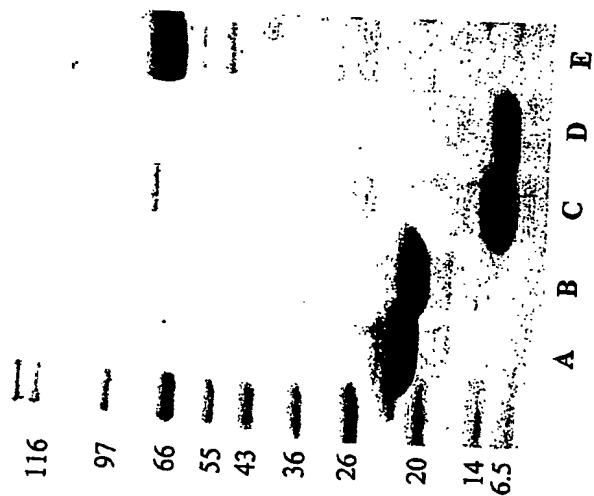


Figure 25

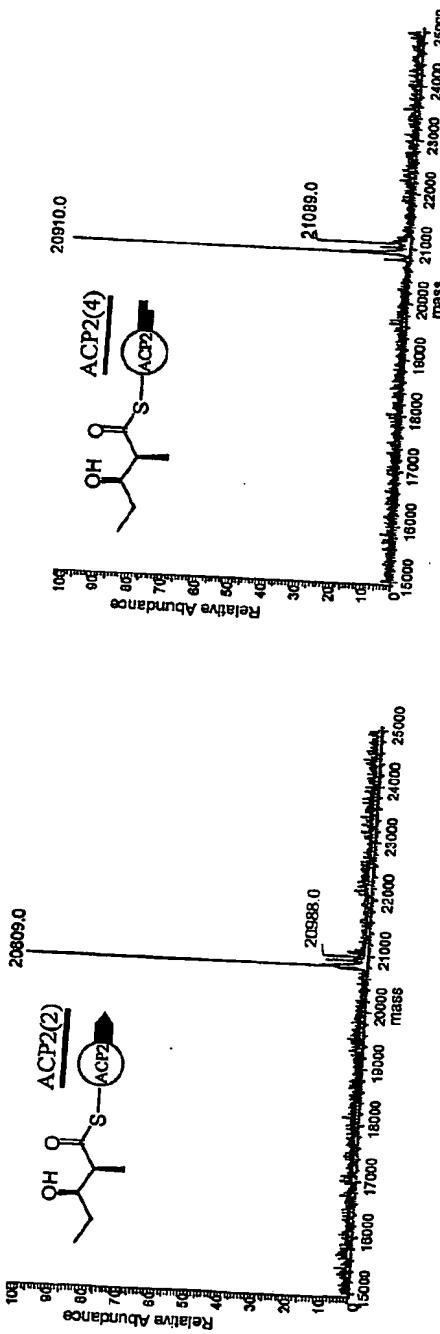
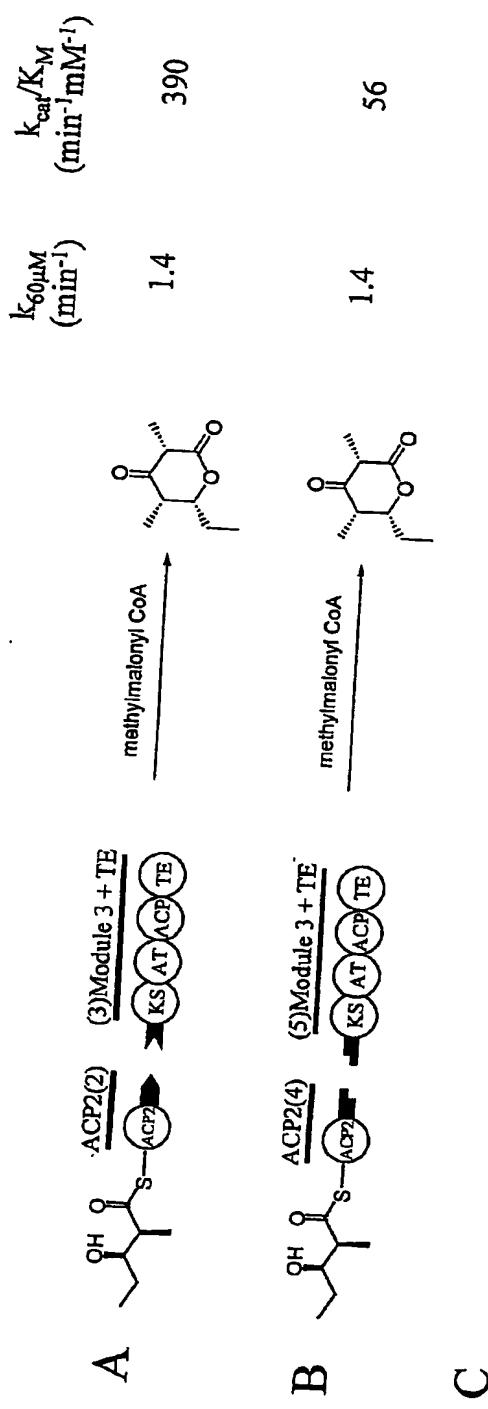


Figure 26

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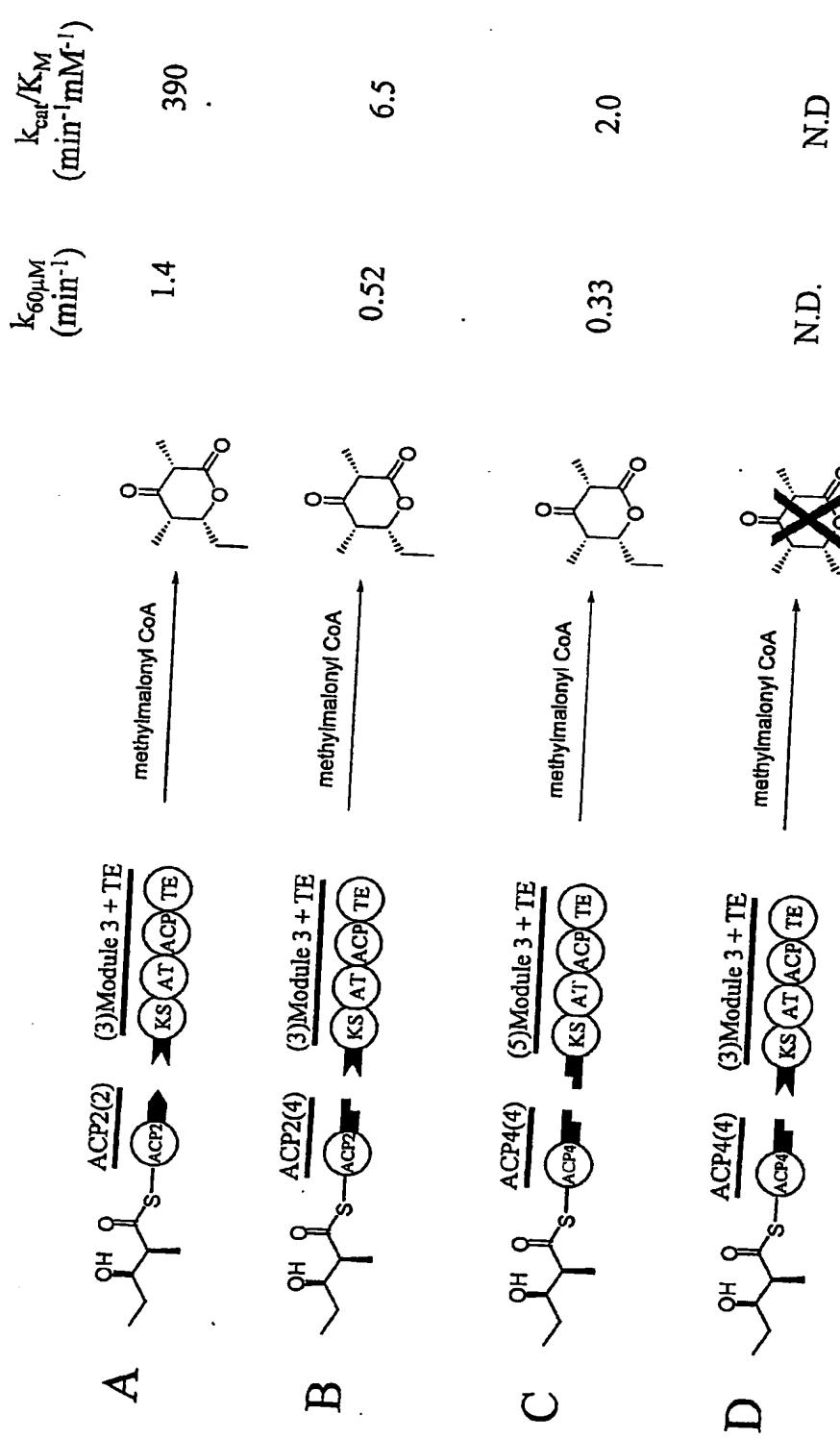


Figure 27

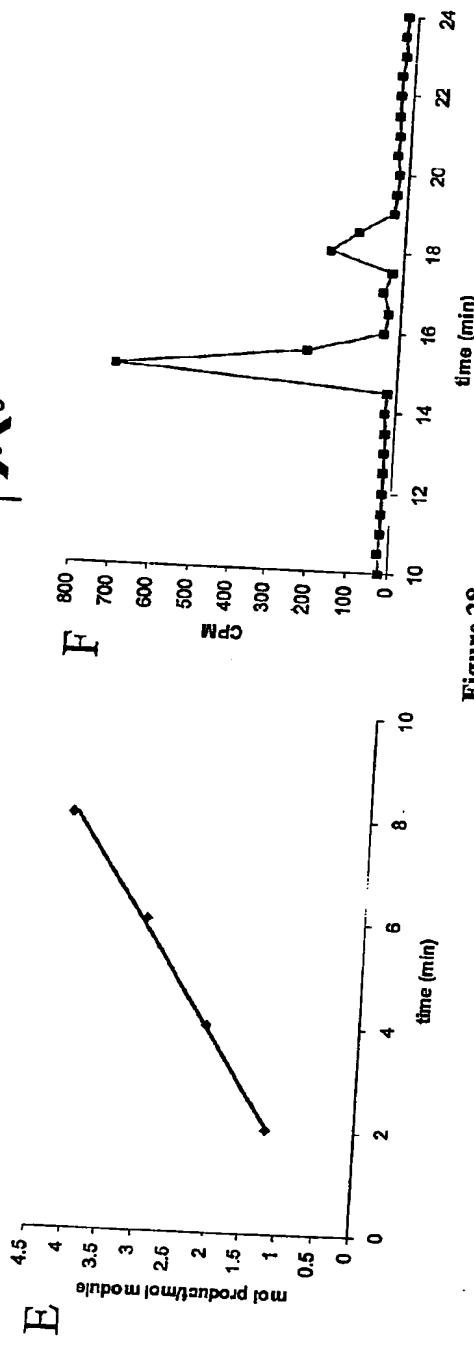
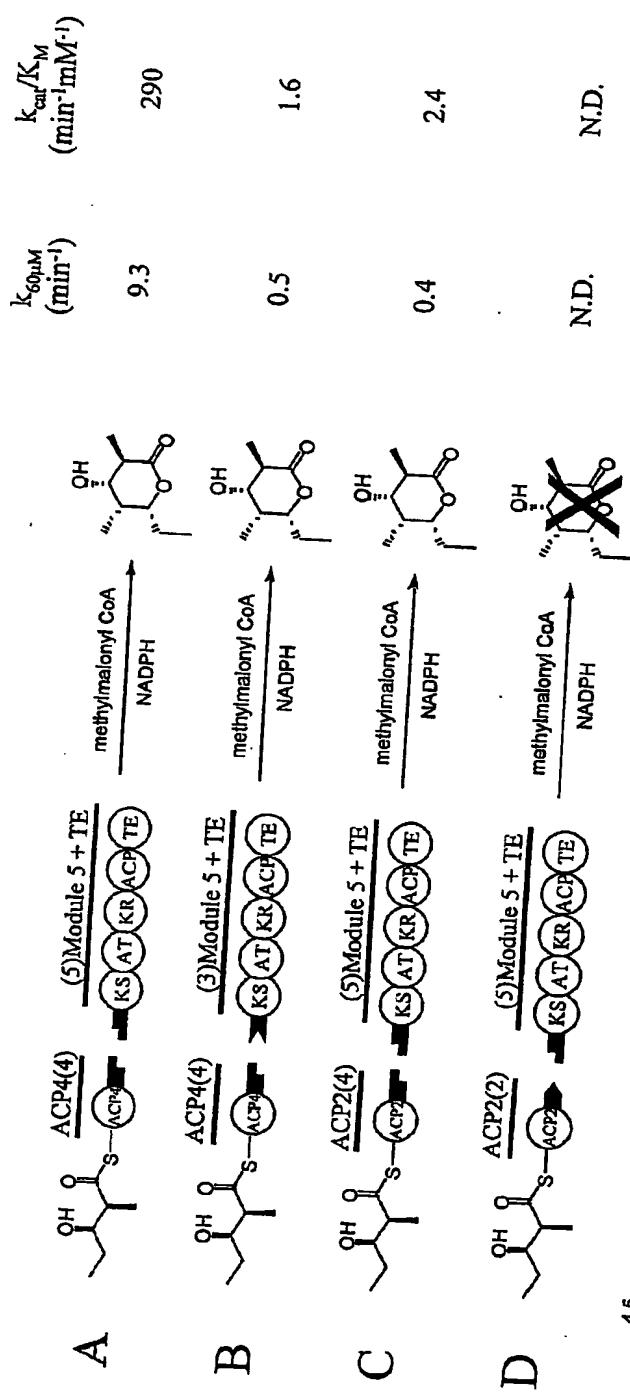


Figure 28

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	k_{cat}/K_m (min ⁻¹ mM ⁻¹)	(min ⁻¹ mM ⁻¹)
A	0.49	4.1
B	0.27	2.5
C	N.D.	N.D.
D	N.D.	N.D.
E	0.44	11
F	0.11	5.2
G	6.7	2900
H	10	340

Figure 29

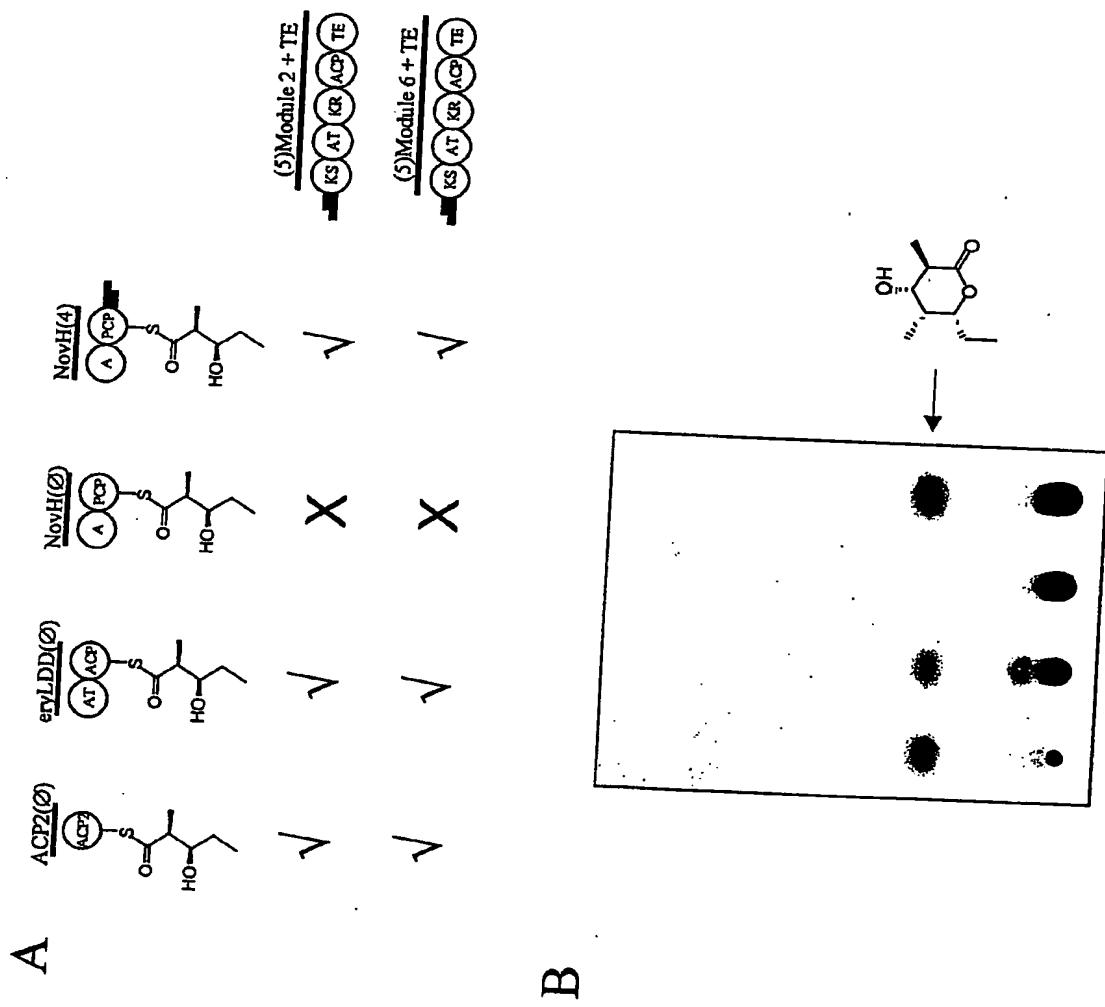


Figure 30

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1	AAPCQHVAWV	AMACRLEGGV	STDEETHEID	SEGRDAVAGL	PTFROWDLDs	LTFEDPFRSC	TABRRGOGES	TEATAIPAE	YNGSERELA	VDEGOSLATE	- 600
2	APVTL-I-I	GMA-L	EV DS-SHIZLH	TSGRSNARV	-D-	VEDE	LAGSD...	A AGTRAH-NEM	AG-GD-A	AG-GD-A	-2071
3	ELEST-I-I	SMA-L	EV DS-SHIZLH	REGGETLSQP	-T-	DILAR	LHFDFDDEPG	TSYVK-GEN	DD-AG-DE	DD-AG-DE	- 126
4	ADESE-I-I	GIG-F	GI GS-SHIZLH	AEGRANLUTGP	-A-	DIGR	LHFDFDDEPG	TSYVK-GEN	TD-AL-PG	TD-AL-PG	-1584
5	HRAGE-I-I	GMA-F	DV DS-SHIZLH	SGGGDAIAEA	-A-	KPD.	...	POARL-GEN	AA-GD-AG	AA-GD-AG	- 122
6	KDADU-I-I	GMA-F	GV HB-SHIZLH	VERGDAVTEH	-T-	DLOA	LFUDOPONH	TSYSRH-ABP	DG-AD-AP	DG-AD-AP	-1581
1	ISGIVIATR	ITPESIHSASP	IGIVEVHDQ	IXGPRPLAEGG	EZEVGILMIG	TTISVASCED	AYMUDHGP	ISVTAICSS	IVAVERPCG	IRGESS-TER	- 700
2	IS-PAV-S-T	ITPESIHSASP	IGIVEVHDQ	IXGPRPLAEGG	EZEVGILMIG	TTISVASCED	AYMUDHGP	ISVTAICSS	IVAVERPCG	IRGESS-TER	-2171
3	IS-PAV-S-T	ITPESIHSASP	IGIVEVHDQ	IXGPRPLAEGG	EZEVGILMIG	TTISVASCED	AYMUDHGP	ISVTAICSS	IVAVERPCG	IRGESS-TER	- 225
4	IS-PAV-S-T	ITPESIHSASP	IGIVEVHDQ	IXGPRPLAEGG	EZEVGILMIG	TTISVASCED	AYMUDHGP	ISVTAICSS	IVAVERPCG	IRGESS-TER	-1684
5	IS-PAV-S-T	ITPESIHSASP	IGIVEVHDQ	IXGPRPLAEGG	EZEVGILMIG	TTISVASCED	AYMUDHGP	ISVTAICSS	IVAVERPCG	IRGESS-TER	- 222
6	IS-PAV-S-T	ITPESIHSASP	IGIVEVHDQ	IXGPRPLAEGG	EZEVGILMIG	TTISVASCED	AYMUDHGP	ISVTAICSS	IVAVERPCG	IRGESS-TER	-1680
1	ASVIVIATR	CMVLFBRMD	SLATVCRCA	SIGNIFC	ISGAGLILRE	RISFRENGH	FLULVHGRC	ISVDAESEN	SNEMGRABVR	VIMGAIASE	- 800
2	AS-MS-AGC	EVFTIE-SROG	S-SPR	SDP	-2271						
3	AS-MS-ATC	EVFTIE-SROG	S-SPR	SDP	- 325						
4	AS-MS-ATC	EVFTIE-SROG	S-SPR	SDP	-1784						
5	AS-MS-ATC	EVFTIE-SROG	S-SPR	SDP	- 322						
6	AS-MS-ATC	EVFTIE-SROG	S-SPR	SDP	-1780						
1	ASVIVIATR	- 898									
2	AS-PAV-VAV	ASVIVIATR	-2371								
3	AS-PAV-VAV	ASVIVIATR	- 425								
4	AS-PAV-VAV	ASVIVIATR	-1882								
5	AS-PAV-VAV	ASVIVIATR	- 422								
6	AS-PAV-VAV	ASVIVIATR	-1880								
1	EPW-BAGARP	- 992									
2	EP-BHAADGV	-2469									
3	EP-BHAADGV	- 818									
4	EP-BHAADGV	-1974									
5	EP-BHAADGV	- 515									
6	EP-BHAADGV	-1978									
S	EPVAPPVDES	- 106									
1	EPVAPPVDES	-1089									
2	EPVAPPVDES	-2559									
3	EPVAPPVDES	- 612									
4	EPVAPPVDES	-2066									
5	EPVAPPVDES	- 603									
6	EPVAPPVDES	-2068									
S	PEQSRERH	- 204									
1	ALSTE-D-V	-1184									
2	APSL-E-D-V	-2659									
3	APGLD-D-V	- 710									
4	DPDHE-D-V	-2164									
5	ARPLD-D-V	- 701									
6	APSL-E-D-V	-2166									
S	VIRG-CHOPES	- 303									
1	EVIA-C-RS	-1284									
2	EVIA-C-RS	-2758									
3	EVIA-C-RS	- 809									
4	EVIA-C-RS	-2263									
5	EVIA-C-RS	- 800									
6	EVIA-C-RS	-2265									
S	FDEATRALS	- 388									
1	AD-VRAHAB	-1381									
2	AD-VRAHAB	-2853									
3	AD-VRAHAB	- 906									
4	AD-VRAHAB	-2358									
5	AD-VRAHAB	- 698									
6	AD-VRAHAB	-2355									
1	LEPKVRAARS	-1439									
2	L...LPDT TP	-2908									
3	ZOPRAPAAA..	- 957									
4	PRPRPRAADS AL	-2592									
5	L...PIFTGG RA	- 952									
6	L...AFB..V	-2399									

Figure 31 A

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1ALEA GARVELVUD ARGGDELAE BIRSV.GR.V AGVLSLLAVD EAEPPEAPLA LASLADTSLVQAMUSA ELCGCPW...	-1516
2ALARA -A.....E PEVTRG VCG LVGCGA... .G-V-LIALE ED..... GAVQTLV-VRELOAE GIDAPIL...	-2964
3AIAN -GRAIRCEVD TSASRTEMAQ AVAQAST.GF RG-L-LISSD ESACR.PGV PAGAVGLA-VQALGAQ GVDAPVU...	-1033
4	AVINTTILEAS -ATSVR-VVA TPGADAMAL RVTIPAGHLV AZ-D-LVVRG TGKWEOPED RGGEGELSA-DNGHLLAEPGS TGRVVAADAS DLDLAVLRSGH	-2691
5GLEQS -ATVLTCDEVE ...SRSTIGT ALRAADTDAL ST-V-LLSRD GEAVD.PSL DA...LA-VQALGAQ GVERAPLN...	-1021
6AVEKA -GRV...VVV ASADREASA LIREVP.GEV AG-L-V..... HSGATHLA-HOSIGEA GVERAPLN...	-2459
1TVI ESWATGPFE RVNTAARGAL NGVGRVIALE HPAWVGGLVD VPAGSVARLA	-1569
2TV FG-DAG.SP .VARPDQAKL N-LGVVASL RGPRTGIVL- LPHPDPDELR	-3015
3CL OG-RTPADD DLAPPAQYH H-FAGVAGL- LPGANGGVU- LPESVDAAL	-1086
4	PEPDADVLRV EPEGDPRAR ARHGVLRAAA LVRRNIEQEE LPGATLVI- SG-TVSDD SVFEPGAAM N-VIRCAOA- SPDRF.VLI- TDAPRG...	-2786
5VL RN-QDAGE LV.DPACQMY G-LGRVGI- QPGRGGLV- LVDA.DASI	-1072
6LV- SR-ALGESE FWDPEADM W-LGVAGL- TPERWGLV- LPAEPAPGDG	-2511
1	RHLAAUVSGG A.GEQLALR ADGTYGBRMV RAAAPA	TIDE.MRPTG FVLMZTQG MGGCMLM ARGPPTD	-1642
2	GRLT-VLAG ..SEDQV-V- ADAVR-LS PAHVT.	ATSEKAV G-I-VSPPG MGRBPLM AGPPTD	-3086
3	RLLV-VLRGG GRAEDHL-V- DGRLLGR-VV BASLPO	SCSRSMH H-V-VSPPG MGRBPLM ADPPTD	-1161
4	.NLP-V... PDNPQL-L- GDDVFVP-LS PLAPSA	TOPAVD D-V-VSPPG MGRBPLM ZEPPTD	-3171
5	RSLA-VLAD PRGEQSV-I- ADGIRVA-LV PAVARA	ARTR.MS-R- V-VSPPG MGRBPLM ARGPPTD	-1145
6	EAFV-CLGAD G.HEDOV-I- DHARYGR-LV RAPLG.	TRESSME A-A-VSPPG MGRBPLM ARGPPTD	-2584
1	VFR-GPDADG AGE/VAELEA HICARTHIAAC MHDRESVRE [REDACTED] ILGGI.GDDV HUSAVEHRA	TLDGHTDYL TGRPHRPER ARGPPTD	-1741
2	WSHNGPDTEG VGD-TAELIT [REDACTED] HGRVSH-C-WSREPREVRE [REDACTED] LIVHGLIEQGD WNG3VV-HAG LPOQVAMNDI DRAPEDEVRA MGRGAVED	HUTRELDITA	-3184
3JAGCR GDD-LAVER HESAVVVC-O HAA...LRE HLGDE..... PVALV-HOT LTEFGSUEV APHEVPLA MGRGAVED	UCSDAEL..	-1248
4	WSHNGADAPG SDE-PARTED HESADEA HEDRDLA HLDL...PFR HUNGVV-HAG VLADGMTSI DEPMONVIR ARGPPTD	MGRNAVER	-3268
5	LHNGADAPG ASE-EELITA HEGVHIA-C HEDRDLA HLAERALEGR HESAVV-HAG VETSTPDDL TEABTEED VHEGTVV-HAG	LTANTGLSF	-3268
6	WSHNGPDAPG AAE-EELVA HEDRDLA HLDREOLSK HLESIRGGR HUTTVV-HAG VPESRHLRI GE.JESSICA A.VNGARL	UCPDLD..A	-1243
1	-2680
1	VFRSSERSA EGAPGLGMA EGAVNLIGLA OGRSGDGLA TAUW-HITVG SGMAEG..AV ADRPRHUVI SPPPTCRA LGRNADRAV CP IVIDVWD	G RENDAEME EGNOISVAM QUPRCAAII	-1639
2HLLV-GV MGSGARQH AAGAS-LPF RNF-GPQH TSVA-EL-A CGM.TGDREAA VSPFLREVR AMVVPF-LAA LGRN-ASGET AVVVDVWD	-3283
3VNSC-GI MGAGHMAA RAGAS-DPL EEE-APRSC TSVA-EL-L PGGAVD..DG ..YLRERL SLSDR-SRT MENV-ASGET SVAVADVWP	-1344
4VNSC-GV DRGQGQH AAGAS-NPL AHS-TPLA RALGCOL-2 ASMTSGLG. .DRIARTVA ALPTE-LAL FISIA-RGGG VVFFLSINRS	-3366
5VNSC-GV HSGSGAS-A AAGAS-DPL HPS-SEAFD TSIA-GL-2 QHAGD..EG GEYLRSCLR AMODDN-VER LRT-DHGT SVSVVMDRR	-1341
6VNSC-GV HSGSGAS-A AAGAS-DPL HPS-SEAFD TSIA-GL-2 KHMAGDLEG ...LTH-LR PMAPER-IRB LGRN-DHGT CUSIADVWD	-2777
1	REFLLAYTAOR PTIHLDEIDD ARAA...EQ APAEPRVGA.	-461
2	APAESYT-AR PRELDRIVT ..TAPSERAG EPETTSILDR L-GLPRAERT AE-VRVRLT'S T-ML-HDP KMPATTI-K R-ML-HDP KMPATTI-V	-1935
3	VLSSEGFA-TR PTIHLDEIDL RGGQARAPD SGPTGEPAOR L-GLSPDQQ EK-LEWANA VHEA-HESA AEINVRRA-S R-ML-HDP KMPATTI-V	-3381
4	ALR...R-EP VEPVERGHRV ARHLRAQQA A.AGNVUDR L-GREEDSDQV AG-RELVSH A-MAS-IGSA DCIPERKA-K R-ML-HDP KMPATTI-V	-1444
5	REFVELFT-AR HRLDEDETAG ARAA...EQ SIEGPALQR L-ALSTAERB EB-ABILRAE V-ML-HDP ANTRDRA-N R-ML-HDP KMPATTI-V	-3462
6	APAVGFT-AR PRELDRIVTPAVGRFVAV O-APARENTS QE-LEPTISH V-ML-HDP ANTRDRA-N R-ML-HDP KMPATTI-V	-1437
1	GRSUNIALLY DHPTRAIED ALAAG	-2866
2	-VHPPTTVF D--DVRTH-A HLAADIGGAT GAEQAAPIATT	-486	
3	-LHPSTLWF D--NASAV-G FLDAE-GTEV RG.EAPSA	-1975	
4	-LHPASLWF D--TTVTA-O HLRD-VG.. DADQAVRVRV GA	-3418	
5	-VHPSTLWF D--TPLAV-E HLRD-PAAS PAVDGDRL ELE	-1484	
6	-VHPATLWF D--TITRQ-D HYL-E-VGAA EAEQAPALVR BVP	-3505	
1	-LHPATLWF E--TVRU-D HIGG-DSGT PAREASSAIR DGY	-1480	
2		-2909	

Figure 31 B

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